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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference SHR503974-142	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/IB2003/002641**	International Filing Date *(day/month/year)* 11 June 2003	Priority Date *(day/month/year)* 11 June 2002
International Patent Classification (IPC) or national classification and IPC **Int. Cl.**[7] G01N 33/68, 33/92, 33/566, 33/74, A61K 38/16		
Applicant AUCKLAND UNISERVICES LIMITED et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheet(s).

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [ ] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [X] Certain observations on the international application

Date of submission of the demand 19 December 2003	Date of completion of the report 8 October 2004
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **ISOBEL TYSON** Telephone No. (02) 6283 2281

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/IB2003/002641

I. Basis of the report

1. With regard to the elements of the international application:*

- [ ] the international application as originally filed.
- [X] the description, pages **1 - 51,** as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [X] the claims, pages **52 -54,** as originally filed,
  pages , as amended (together with any statement) under Article 19,
  pages , filed with the demand,
  pages **55, 56,** received on **10 November 2003** with the letter of **19 December 2003**
- [X] the drawings, pages **1/15 - 15/15,** as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the sequence listing part of the description:
  pages , as originally filed
  pages , filed with the demand
  pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [ ] the language of publication of the international application (under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- [ ] contained in the international application in written form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form.
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	**YES**
	Claims **1-33**	**NO**
Inventive step (IS)	Claims	**YES**
	Claims **1-33**	**NO**
Industrial applicability (IA)	Claims **1-33**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

This report is based on the following documents:

- MacNeil DJ et al (2002). The role of melanocortins in body weight regulation: opportunities for the treatment of obesity. *European Journal of Pharmacology* **440:** 141-157, published 12 April 2002 **- (New citation)**
- US 6310034 A (WOYCHIK et al), 30 October 2001
- WO 199931508 A (MERCK & CO INC), 24 June 1999
- www.phoenixpeptides.com – **(New citation)**

NOVELTY (N) AND INVENTIVE STEP (IS):

Claims 1 to 33 are not novel and not inventive in the light of the following documents, despite the comments in the response relating to agouti proteins. Alpha MSH peptide is a melanocortin that is an agonist peptide ligand for the melanocortin receptors (claims 7, 14, 16 etc). It is well known and has been available commercially in Australia for research since 1999. See also catalogue from earlier second opinion which discloses the commercial sale of alpha-MSH in Australia (by Australian Laboratory Services). Its therapeutic use in obesity research in humans is also well known -see the citations **(b)** to **(e)** below. The composition has been defined by its intended use rather than its constituents. Therefore, claims 1 to 33 are not novel in the light of:

(a) the commercial availability of alpha-MSH in Australia before the filing date for use in obesity research (see above);

(b) MacNeil DJ et al:
This document discloses the role of melanocortins in body weight regulation and suggests them as treatment for obesity and addresses therapeutic applications including the role of food intake and energy expenditure – see in particular page 145 lines 38 to 48, lines 38 to 41 and section 4.2, section 5.1, page 149, section 6 page 150-151, page 153 paragraph 1;

(c) US 6310034:
This document discloses the well known effect of targeted disruption of melanocortin peptide on obesity, for example, see column 142; and

(d) WO 199931508:
This document discloses the use of polypeptide inhibitors of the binding of MSH to melanocortin receptors to control obesity. Regulation of MSH is known to have a role in the control of feeding behaviour and obesity, for example see page 1 line 17 to page 2 line 31.

CONTINUED ON SUPPLEMENTAL SHEET:

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The applicant may wish to correct typographical errors in the specification, for example page 14 line 15, "[," and page 52 line 9.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V(2):

The difference between the claimed invention and the citations resides only in a variation on the prior art use of the compound in obesity regulation and its known role in the therapeutic treatment of obesity. The described invention should be characterised by its components and not by its intended use. The claimed invention does not derive novelty merely through claiming variations on its use as a known compound in its known therapeutic use for obesity. Claims 1 to 33 are therefore deprived of novelty and invention in the light of the above citations.

I also refer you to **(e)** www.phoenixpeptides.com which discloses the sale of obesity regulating melanocortin peptides, by Phoenix Pharmaceuticals, Inc. The current site is copyrighted from 2003, however, which is after the filing date of the proposed invention relating to a method of use of the melanocortin peptides.

Documents **(f)** WO 199921571 A (TREGA BIOSCIENCES, INC), 6 May 1999 and **(g)** PubMed Abstract NIPPON RINSHO. 2002 Feb; 60(2): 404-9 PMID: 11857934 SHINTANI M et al are considered to be background art, relating in part to abnormalities in melanocortin-4 receptor peptide induced obesity.

INDUSTRIAL APPLICABILITY (IA):

No issues of lack of industrial applicability arise.

feeding/weight gain pattern in a subject comprising analysing the profile of response parameters in a sample from a test subject by comparing it with

(i) the profile of a sample from a normal subject and

(ii) the profile of a sample from an obese subject or a subject with an imbalance in energy homeostasis and/or disturbance in feeding/weight gain pattern,

wherein resemblance of the profile of the sample obtained from the test subject to that of the profile in (ii) above, is indicative of that subject being at risk of developing obesity or developing and/or having an imbalance in energy homeostasis and/or disturbance in feeding/weight gain pattern.

23. A method according to any one of claims 1 to 22, wherein the subject is a mammal.

24. Method of determining the melanocortin peptide status of a sample comprising contacting the sample with a biological response system wherein the resulting profile of response parameters produced by the biological response system indicates the melanocortin peptide status of the sample.

25. A method according to any one of claims 1 to 24, wherein the sample is a biological fluid selected from the group consisting of whole blood, plasma, serum, saliva, sweat, urine, amniotic fluid, cord blood and cerebrospinal fluid.

26. Method of screening for a compound which acts as agonist or antagonist of a melanocortin receptor comprising treating a biological response system with a test compound and measuring the resulting profile of response parameters that are indicative of agonist or antagonist activity to the melanocortin receptor.

27. Method of screening for a compound that is useful in the treatment of obesity comprising exposing a biological response system to a test compound and measuring the resulting profile of response parameters that are indicative of the desired response for the treatment of obesity.

28. Method of screening for a compound that is useful in the treatment of an imbalance in energy homeostasis or a disturbance in feeding/weight gain patterns comprising exposing a biological response system to a test compound and measuring the resulting profile of response parameters that are indicative of the desired response for the treatment of an imbalance in energy homeostasis or a disturbance in feeding/weight gain patterns.

29. A method according to any one of claims 15 or 21 to 28, wherein the biological response system is an *in vitro* cell, organ or tissue sample, or whole animal capable of responding to melanocortin peptides.

30. A method according to claim 29, wherein the *in vitro* cell is selected from the group consisting of primary osteoblasts, osteosarcoma cell line, hypothalamic cell line, adipocytes, myocytes, melanoma cells and anterior pituitary cells.

31. A method according to claim 29, wherein the organ or tissue sample is that of hypothalamus.

32. A method according to any one of claims 15 or 21 to 31, wherein the profile of response parameters measured comprise one or more proteins or cellular events which differentiate between normal subjects and those at risk of developing obesity or having obesity, or those with an imbalance in energy homeostasis, or disturbance in feeding/weight gain patterns.

33. A method according to claim 32, wherein the one or more proteins are selected from the group consisting of heat shock protein homologue, glyceraldehyde-3-phosphate-dehydrogenase, aldo-keto reductase, citrate synthase, creatine kinase, pyruvate synthase alpha-chain, f1 ATPase beta-chain, tubulin beta-chain, proteins involved in the melanocortin peptidergic axis, proteins involved in signalling pathways and membrane-bound proteins.